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CT-scan based liver and spleen volume measurement as a prognostic indicator for patients with cirrhosis

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Abstract

Background: Complications of patients with liver disease generally occurs as the consequence of advanced fibrosis and portal hypertension. Non-invasive tools to predict the complications may allow for better risk-stratification and medical management in patients with cirrhosis. The goals of this study are to determine the utility of CT-scan based liver and spleen volume measurement in association with complications and outcomes in patients with cirrhosis.

Methods: Baseline demographic and clinical characteristics of 556 cirrhotic patients who underwent CT scan of the abdomen between January 1-June 30,2009 were reviewed. Liver and spleen volume were measured using semi-automated interactive software and compared to 47 healthy controls. The association between liver and spleen volume and complications of cirrhosis was determined. Independent predictors of survival were analyzed with Cox regression model.

Results: Patients with cirrhosis had significantly lower total and functional liver volume, larger total and functional spleen volume, and significantly lower total liver to spleen volume ratio when compared to controls. Liver volume, spleen volume, and liver to spleen volume ratio were

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Authors' contribution

MP collected the data. MP, MT, and SL reviewed the data, wrote the manuscript and edited the manuscript.

Ethics approval and consent to participate

The study is approved by the Institutional Review Board at Indiana University School of Medicine which abides by the guidance of the Declaration of Helsinki. This was a minimal risk study and consent requirements waived as a result. IRB number 1503966995

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality of human research data from our institution, but are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

significantly altered in patients with decompensated stage. Patients with hepatic encephalopathy had significantly lower total liver volume and spleen size was associated with the presence of esophageal varices. Cirrhotic patients who underwent liver transplantation had significantly lower total liver volume and larger total spleen volume. However, spleen volume was not an independent predictor for mortality.

Conclusion: Baseline liver and spleen volume and its ratio are significantly altered in patients with cirrhosis. Spleen volume is also associated with the presence of esophageal varices.

Keywords

spleen volume; cirrhosis; esophageal varices

Background

Liver cirrhosis, the advanced stage of hepatic fibrosis, may result in serious complications including hepatic encephalopathy, thrombocytopenia, ascites, and esophageal or gastric varices secondary to portal hypertension.[1,2] These complications, known as decompensated stage, are associated with high mortality[3] Recognizing and understanding the various complications of decompensated cirrhosis may lead to better risk-stratification and improve clinical outcomes.

Liver biopsy is the gold standard to diagnose and evaluate the severity of fibrosis in cirrhosis.[4] Given the invasive nature of the procedure with bleeding and other procedure-related complications, non-invasive tests to screen for the presence of advanced fibrosis have been utilized to prognosticate or predict the likelihood of complications in patients with decompensated cirrhosis. Fibrosis-4 (FIB-4) is a non-invasive test based on the patient's age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count. Its level is associated with the severity of fibrosis in cirrhosis patients.[5] Transient elastography is a tool to determine underlying fibrosis in patients with liver disease. It requires equipment and is operator dependent[6].

Imaging modalities such as computed tomography (CT) have been able to identify factors related to complications secondary to cirrhosis.[7] The use of platelet count with total liver volume, right liver volume (RLV) and spleen volume (SV) has been shown to be correlated with Child-Pugh class and of the presence of esophageal varices.[8–11] Spleen stiffness is associated with the size of esophageal varices.[12,13] The ratio of liver to spleen ratio is an indicative of cirrhosis progression and a predictor of complications in patients after hepatectomy and those with primary biliary cholangitis[14].[15] However, common to most of these studies is a small study sample preventing analysis of the various etiologies of cirrhosis and absence in the analysis examining the prognostic significance of spleen volume in patients with cirrhosis.

The objectives of our study are 1) to compare liver and spleen volume as well as its ratio in patients with cirrhosis to body-weight matched controls, 2) to determine if there is an association between spleen volume or liver to spleen volume ratio with the complications

secondary to portal hypertension, and 3) to assess if spleen volume is a prognostic indicator for mortality and long-term outcomes in patients with cirrhosis.

Methods

Study cohort

CT scan imaging of 568 patients with cirrhosis and no known history of hepatocellular carcinoma who received their clinical care at Liver clinic, Indiana University between January 1-June 30, 2009 were retrospectively identified. CT scan was performed as part of hepatocellular carcinoma surveillance.Baseline characteristics, clinical course of liver disease (presence of absence of hepatic encephalopathy, esophageal varices, or ascites), laboratory tests (within 2 weeks from the date of CT scan), upper endoscopy results, Child-Pugh classification, and MELD scores were extracted from medical records. Of these, 12 patients were excluded due to missing information on baseline labs or baseline body weight. A total of 556 patients constituted the study cohort. We also identified 47 healthy controls with age-, gender-, and BMI-matched to those with cirrhosis. The schematic diagram of patient selection is shown in Supplementary Figure 1. The study was approved by the Institutional Review Board at the Indiana University Purdue University Indianapolis (IUPUI).

CT scan-based liver (LV) and spleen volume (SV) measurement

Liver volume (LV) measurement was performed as previously described[11]. Spleen volume (SV) measurement was determined using the semi-automated interactive software "IntelliSpace Portal Liver Analysis application" (Philips Medical Systems, Best, The Netherland). Manual placement of the location of the spleen was conducted allowing the software to identify spleen contour and volume (Supplementary Figure 2). Functional spleen volume was measured by subtracting total spleen volume from the volume of splenic vessels. The measurement was completed independently by MT and MP. The association of the volume measurement for both readers was shown in Supplementary Figure 3, with calculated Pearson correlation coefficient at 0.97 and Spearman Correlation at 0.97.

Statistical analysis

Mean, standard deviation (SD) and frequencies (percentages) were characterized from the data set. Analyses were conducted utilizing SAS software version 9.4 (SAS Institute, Cary, NC). Chi-square test, Student t test, or analysis of variance (ANOVA) was used. The evaluation of independent predictors for mortality was conducted using Cox proportional hazards model. P-value less than 0.05 was considered statistically significant.

Results

Baseline characteristics of study population

Baseline clinical characteristics of our study cohorts are presented in Table 1. According to the study design, there was no differences in age, gender, race, and BMI between both groups. Patients with cirrhosis had a significantly higher level of creatinine (1.1 vs 0.9 mg/dl, p=0.001), alanine aminotransferase (ALT) (54.1 vs 22.5 IU/L, p=<0.0001), aspartate

aminotransferase (AST) (78.0 vs 20.7 IU/L, p=<0.001), alkaline phosphatase (ALP) (132.4 vs 83.5 IU/L, p=<0.001), and a lower albumin (3.0 vs 4.1 g/dl, p=<0.001).

Liver to spleen volume ratio and spleen volume in patients with cirrhosis stratified by etiologies

Patients with cirrhosis were noted to have a significantly lower liver to spleen volume ratio when compared to controls (3.15 vs 9.98, p<0.0001) (Table 1). When we considered this ratio based on the etiologies of underlying cirrhosis, we found that non-alcoholic steatohepatitis (NASH) patients had significantly lower liver to spleen volume ratio (2.17) compared to that for patients with hepatitis C (3.2), alcoholic cirrhosis (3.5), and hepatitis C and alcohol (3.3) (Table 2). Patients with cirrhosis had significantly larger spleen compared to controls (796.2 cm^3 vs 218.3 cm^3, p=<0.0001) (Table 1). When we calculated the spleen volume stratified by etiologies of underlying liver disease, we found that NASH patients had the largest splenic size (934.5 cm^3) (Table 2).

Liver to spleen volume ratio and spleen volume in patients with cirrhosis stratified by compensatory stages

We determined the differences in the liver to spleen volume ratio and spleen volume in compensated (Child –Pugh Class A) and decompensated (Child-Pugh Class B and C) patients (Table 3). As expected, we found that patients with decompensated stage had significantly lower level of hemoglobin (12.0 vs. 13.4 g/dl, p=0.001) and platelets (104.7 vs. 122.1 cells/mm^3, p=0.007) compared to those with compensated stage. Patients in decompensated stage had higher MELD scores (13.4 vs. 8.4, p<0.0001).

Patients with decompensated stage had significantly lower liver volume (1574.7 vs. 1754 cm^3, p=0.0005). The detailed information of liver volume by hepatic segment is shown in Table 3. Patients with decompensated stage had a larger spleen size with the average volume of 864.8 cm^3 compared to that of 676.0 cm^3 for those with compensated stage (p<0.0001). The liver to spleen volume ratio was significantly lower in patients with decompensated stage (2.7 vs. 4.0, p<0.0001). The complete information for liver to spleen volume ratio and spleen volume stratified by each Child-Pugh class is shown in Supplementary Table 1.

Liver to spleen volume ratio and spleen volume in association with the complications from portal hypertension

We next determined if liver to spleen volume ratio and spleen volume are associated with the complications of portal hypertension, hepatic encephalopathy, esophageal varices, and ascites (Table 4). For hepatic encephalopathy (HE), we found that those with history of HE had significantly lower total liver volume (1509 vs. 1695 cm^3, p=0.002) and functional liver volume (1481 vs. 1638 cm^3, p=0.007) compared to those without history of HE. We did not observe the differences between total liver and functional liver volume between those with and without esophageal varices or ascites (Table 4). There was no difference in spleen volume in patients with and without history of HE or ascites. However, patients with history of esophageal varices had significantly larger total spleen volume (893 vs. 683 cm^3, p<0.0001) and functional spleen volume (661.4 vs. 868.2 cm^3, p<0.0001). Interesting, we

found significant differences in the liver to spleen volume ratio in patients with and without history of ascites (2.7 vs. 3.5, p=0.01).

Liver to spleen volume ratio and spleen volume and outcomes in patients with cirrhosis

During the median follow up period of 3.1 years, 111 underwent liver transplantation and 126 died. Patients who underwent liver transplantation were younger (53.4 vs. 55.7 yrs, p=0.03) than those who were alive. For those who were transplanted, they had significantly lower total liver volume (1514.8 vs. 1736.4 cm^3, p=0.0004), lower functional liver volume (1482 vs. 1676 cm^3, p=0.001), and larger total spleen volume (946.9 vs. 778.9 cm^3, p=0.008)(Table 5). Total liver to spleen volume ratio was also significantly lower in those who underwent liver transplantation (2.2 vs. 3.3, p<0.001)(Table 5). We also performed Cox proportional hazard model and found that only age (p=0.006) and MELD scores (p=<0.0001), but not the splenic volume, were independently associated with mortality. Detailed information on the liver and spleen volume in association with the outcomes is shown in Supplementary Table 2.

Discussion

In this study, we found that patients with cirrhosis had significantly lower total and functional liver volume, larger total and functional spleen volume, and as a consequence, a significantly lower total liver to spleen volume ratio when compared to healthy controls. While we did not find the association between total liver volume and underlying etiologies of cirrhosis, we observed that NASH patients had the largest spleen size compared to those with liver diseases from other etiologies. Liver volume, spleen volume, and liver to spleen volume ratio were significantly altered in patients with decompensated stage. Patients with HE had significantly lower total liver volume and spleen size was associated with the presence of esophageal varices. Lastly, we found cirrhotic patients who underwent liver transplantation had significantly lower total liver volume, lower functional liver volume, and larger total spleen volume. However, spleen volume was not an independent predictor for mortality.

The complications secondary to underlying chronic liver diseases occur as a consequence of underlying fibrosis. While the gold standard to quantity the severity of underlying fibrosis requires liver biopsy, the potential complications associated with the procedure prohibits its routine use in clinical practice. At present, there are several non-invasive biological tests, such as FIB-4, AST to platelet ratio index, or enhanced liver fibrosis test to assess the severity of liver fibrosis in those with chronic liver disease[6]. Transient elastography to measure the liver stiffness is increasingly used as a noninvasive tool for fibrosis assessment[6]. Patients with advanced liver disease or cirrhosis generally undergo radiographic imaging such as CT scan for hepatocellular carcinoma surveillance. Given the readily available semi-automated interactive software, we set out this study to determine if the measurement of liver and spleen volume will be useful as an indirect indicator for the care of patients with cirrhosis. Liver volume has been used as a pre-operative assessment and risk stratification for patients undergoing hepatic resection. Baseline liver volume is associated with post-operative morbidity and mortality[16]. We found that liver volume of patients with

cirrhosis was significantly lower than that of normal healthy controls. It is known that splenomegaly as a consequence of portal hypertension is common in patients with cirrhosis; the observation which is confirmed in our study with the measurement of a total spleen volume. Of importance, the size of liver and spleen is associated with specific complications of portal hypertension. We found that liver size is associated with the presence of hepatic encephalopathy while the spleen volume is associated with the presence of esophageal varices. Our finding confirmed the previous observation that splenomegaly detected by CT scan or by physical examination is an independent predictor of large esophageal varices[17]. Recently, a composite score based on the presence of acute upper gastrointestinal bleeding, ascites, and platelet counts, known as Liaoning score, was developed and validated as a predicting tool of esophageal varices in patients with cirrhosis[18,19]. This scoring system is based on readily available clinical and laboratory data with the good diagnostic performance for esophageal varices[18,19]. We attempted to determine the diagnostic ability of spleen volume with that of Liaoning score; unfortunately, our data did not capture the presence of acute bleeding status. Future studies to explore several non-invasive tools based on clinical, laboratory, and radiographic data should be explored. We previously reported the important role of liver volume and mortality of patients with cirrhosis[11]. However, it did not appear that the spleen volume has any prognostic significance on mortality in these patients. A recent study using CT-based value by measuring liver to abdominal area ratio (LAAR) was reported in 128 cirrhotic patients with Child-Pugh Class B or C[20]. This ratio is effective for predicting the in-hospital mortality[20]. It will be of interest to determine if using the combination parameters as reported in our study when compared to LAAR will improve the prognostic outcomes in these patients.

The strengths of our study are the large sample size with prospective follow up data on the outcomes. We also acknowledged the limitation on the nature of the retrospective study design and lack of validation cohort in our study. While we found that patients with NASH had the largest spleen size compared to those with cirrhosis from other etiologies, it is important to note that we did not account for the severity of underlying cirrhosis and it is plausible that NASH patients had more advanced disease. Nonetheless, we believe that our results are clinically relevant on the utilization of liver to spleen volume ratio and spleen volume in patients with cirrhosis.

In conclusion, baseline liver and spleen volume and its ratio are significantly altered in patients with cirrhosis. Spleen volume is also associated with the presence of esophageal varices. Our results suggest that the measurement of such values may be beneficial specifically to cirrhotic patients who have clinically indicated indication for CT radiographic examination of the liver. If externally validated, these values may be useful to be considered as part of radiographic report in such patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of abbreviations:

ANOVA	analysis of variance
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BMI	body mass index
CT	computed tomography
HCC	hepatocellular carcinoma
MELD	Model for end stage liver disease
NASH	non-alcoholic steatohepatitis
RLV	right liver volume
SD	Standard deviation
SV	Splenic volume

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Table 1:

Baseline characteristics, laboratory values, and liver volume measurements in controls and patients with cirrhosis

Variables	Controls (N=47)	Cirrhosis (N=556)	p-value
Age (Yrs)	52.2±7.5	55.8±10.1	0.71
Gender (Men, n %)	23 (49%)	339 (61%)	0.10
Race (Whites, n %)	41 (87%)	500 (89%)	0.71
Body weight (Kg)	85.0±18.4	87.1±21.3	0.46
Height (cm)	170.5±12.2	170.7±13.0	0.92
Body mass index (kg/m^2)	29.6±6.8	30.2±11.0	0.59
White blood cell counts (×10^3/mm^3)	10.3±4.5	5.8±3.4	<0.0001
Hemoglobin (g/dl)	13.6±1.8	12.5±5.9	0.002
Platelet counts (×10^3/mm^3)	276.4±101.2	111.1±77.2	<0.0001
Blood urea nitrogen (mg/dl)	13.4±5.8	15.0±12.5	0.10
Creatinine (mg/dl)	0.9±0.2	1.1±1.5	0.0001
Total bilirubin (mg/dl)	1.5±5.8	2.6±3.3	0.21
Alanine aminotransferase (ALT, U/L)	22.5±15.6	54.1±87.0	<0.0001
Aspartate aminotransferase (AST, U/L)	20.7±10.7	78.0±108.7	<0.0001
Alkaline phosphatase (ALP, U/L)	83.5±30.8	132.4±108.4	<0.0001
Albumin (g/dl)	4.1±0.4	3.0±0.7	<0.0001
Total protein (g/dl)	7.3±0.6	7.1±3.2	0.34
International normalized ratio (INR)	1.1±0.7	1.7±6.9	0.06
MELD scores	N/A	11.6±7.0	<0.0001
Total liver volume (TLV, cm^3)	1789.5±421.1	1639.8±594.5	0.02
Functional liver volume (FLV, cm^3)	1728.4±413.4	1589.4±579.8	0.03
Portal vein volume (PVV, cm^3)	33.5±18.8	29.1±29.7	0.15
Segment 1 volume (cm^3)	40.2±20.6	46.0±47.9	0.11
Segment 2 volume (cm^3)	214.9±78.7	257.7±189.8	0.002
Segment 3 volume (cm^3)	124.1±80.6	184.0±139.5	<0.0001
Segment 4 volume (cm^3)	293.2±101.6	249.2±155.6	0.0006
Segment 5 volume (cm^3)	296.0±118.5	230.3±140.9	0.0007
Segment 6 volume (cm^3)	177.3±92.5	167.4±164.8	0.51
Segment 7 volume (cm^3)	272.8±99.6	250.7±126.4	0.15
Segment 8 volume (cm^3)	310.3±104.7	231.2±103.5	<0.0001
Total spleen volume (cm^3)	218.3±105.4	796.2±508.5	<0.0001
Functional spleen volume (cm^3)	214.0±102.0	771.4±493.6	<0.0001
Total liver to spleen ratio	9.98±5.2	3.15±3.1	<0.0001
Functional liver to spleen ratio	9.77±5.0	3.16±3.2	<0.0001

Table 2.

Liver volumes stratified by underlying etiologies of cirrhosis

Variables	Hepatitis C (N=138)	Alcohol (N=84)	Hepatitis C+alcohol (N=59)	NASH (N=69)	p-value
Total liver volume (TLV, cm^3)	1668.3±507.4	1593.7±634.3	1758.5±585.3	1566.9±560.9	0.20
Functional liver volume (FLV, cm^3)	1606.6±510.1	1556.5±609.7	1710.2±570.9	1542.0±523.7	0.29
TLV:BW (cm^3:kg)	19.3±5.9	19.6±7.8	20.3±1.4	18.4±14.2	0.63
FLV:BW (cm^3:kg)	18.6±5.8	19.2±7.5	19.8±6.4	18.1±13.7	0.66
Segment 1 (cm^3)	50.5±52.2	46.4±46.5	45.2±38.5	50.1±47.7	0.86
Segment 2 (cm^3)	280.9±312.2	222.6±91.0	279.1±131.8	245.4±121.3	0.20
Segment 3 (cm^3)	204.6±177.7	156.6±107.0	190.5±126.8	178.4±129.6	0.11
Segment 4 (cm^3)	235.5±123.4	250.2±131.4	297.4±232.3	261.4±140.6	0.07
Segment 5 (cm^3)	232.6±130.6	232.4±134.3	239.3±115.6	222.6±125.3	0.90
Segment 6 (cm^3)	179.6±133.0	179.7±258.6	160.9±97.2	138.9±79.8	0.32
Segment 7 (cm^3)	247.0±97.9	261.4±152.5	266.7±106.2	227.1±94.0	0.17
Segment 8 (cm^3)	234.3±97.1	216.0±112.9	251.2±119.0	211.3±82.0	0.09
Total spleen volume (cm^3)	789.4±517.5	647.1±350.0	856.4±621.6	934.5±471.5	0.003
Functional spleen volume (cm^3)	764.5±500.1	628.6±341.8	830.4±603.7	908.8±458.1	0.003
Total liver to spleen ratio	3.2±2.5	3.5±3.8	3.3±2.4	2.17±1.5	0.01
Functional liver to spleen ratio	3.2±2.5	3.5±3.7	3.3±2.4	2.15±1.5	0.01

Table 3:

Baseline characteristics, laboratory values, and liver and spleen volume measurements stratified by Child Pugh Classification.

Variables	Compensated stage Child Class A (N=202)	Decompensated stage Child Class B and C (N=354)	p-value
Age (Yrs)	56.4±10.4	55.5±9.9	0.35
Body weight (Kg)	85.4±19.2	88.0±22.3	0.14
Height (cm)	169.7±13.1	171.3±12.9	0.17
Body mass index (kg/m^2)	29.4±6.3	30.6±12.9	0.11
White blood cell counts (×10^3/mm^3)	5.6±3.5	5.8±3.2	0.37
Hemoglobin (g/dl)	13.4±6.2	12.0±7.0	0.001
Platelet counts (×10^3/mm^3)	122.1±66.6	104.7±82.1	0.007
Blood urea nitrogen (mg/dl)	14.5±8.8	15.3±14.2	0.42
Creatinine (mg/dl)	1.2±1.5	1.1±1.4	0.25
Total bilirubin (mg/dl)	1.2±0.5	3.4±3.9	<0.0001
Alanine aminotransferase (ALT, U/L)	48.4±44.7	57.3±103.8	0.16
Aspartate aminotransferase (AST, U/L)	55.2±45.2	91.1±130.4	<0.001
Alkaline phosphatase (ALP, U/L)	110.9±70.7	145.0±123.7	<0.0001
Albumin (g/dl)	3.6±0.5	2.7±0.5	<0.0001
Total protein (g/dl)	7.6±5.2	6.8±0.9	0.02
International normalized ratio (INR)	1.2±0.1	1.9±0.45	0.06
MELD scores	8.4±5.0	13.4±7.3	<0.0001
Total liver volume (TLV, cm^3)	1754.0±562.3	1574.7±603.2	0.0005
Functional liver volume (FLV, cm^3)	1676.9±573.4	1539.5±578.2	0.007
Segment 1 volume (cm^3)	48.2±47.5	44.7±48.0	0.41
Segment 2 volume (cm^3)	271.4±266.8	249.8±126.0	0.28
Segment 3 volume (cm^3)	209.0±175.4	169.8±112.2	0.004
Segment 4 volume (cm^3)	262.2±150.9	241.7±158.0	0.13
Segment 5 volume (cm^3)	255.6±170.5	216.1±119.0	0.004
Segment 6 volume (cm^3)	177.6±109.1	161.6±189.8	0.20
Segment 7 volume (cm^3)	263.7±112.8	243.4±133.0	0.058
Segment 8 volume (cm^3)	242.7±100.0	224.5±105.0	0.04
Total volume:body weight (cm^3:kg)	21.1±7.1	18.7±9.3	0.0009
functional volume:body weight (cm^3:kg)	20.2±7.1	18.3±8.9	0.007
Segment 1:BW (cm^3/kg)	0.6±0.6	0.5±0.5	0.26
Segment 2:BW (cm^3/kg)	3.2±2.5	2.9±1.9	0.33
Segment 3:BW (cm^3/kg)	2.5±2.1	2.1±1.7	0.008
Segment 4:BW (cm^3/kg)	3.2±1.9	2.8±2.1	0.07
Segment 5:BW (cm^3/kg)	3.1±2.0	2.6±1.6	0.003

Variables	Compensated stage Child Class A (N=202)	Decompensated stage Child Class B and C (N=354)	p-value
Segment 6:BW (cm^3/kg)	2.1±1.3	1.9±2.0	0.11
Segment 7:BW (cm^3/kg)	3.2±1.5	2.9±1.7	0.03
Segment 8:BW (cm^3/kg)	2.0±1.2	2.6±1.3	0.02
Total spleen volume (cm^3)	676.0±440.7	864.8±531.9	<0.0001
Functional spleen volume (cm^3)	655.3±427.8	837.6±516.5	<0.0001
Total spleen volume:BW (cm^3/kg)	7.9±5.0	10.3±7.6	<0.0001
Functional spleen volume:BW (cm^3/kg)	7.6±4.9	9.9±7.3	<0.0001
Total liver to spleen ratio	4.0±2.9	2.7±3.2	<0.0001
Functional liver to spleen ratio	3.9±2.8	2.7±3.2	<0.0001

Table 4.

Liver and spleen volumes stratified by baseline complications of portal hypertensions *

Variables	Hepatic encephalopathy			Esophageal varices			Ascites		
	Yes (N = 120)	No (N= 274)	p-value	Yes (N=142)	No (N=248)	p-value	Yes (N=89)	No (N=285)	p-value
Liver volume without bodyweight adjustment									
Total liver volume (TLV, cm^3)	1509.9±515.7	1695.0±617.7	0.002	1622.3±564.3	1651.1±614.3	0.63	1598.3±564.3	1665.8±591.7	0.33
Functional liver volume (FLV, cm^3)	1481.4±488.6	1638.4±604.9	0.007	1580.4±548.6	1599.4±595.0	0.74	1550.9±553.0	1617.2±571.4	0.32
Segment 1 (cm^3)	44.9±41.1	51.6±45.5	0.17	48.2±42.0	50.8±51.4	0.60	42.8±40.4	52.4±50.2	0.07
Segment 2 (cm^3)	253.9±130.5	263.0±237.2	0.62	256.9±111.3	262.3±251.8	0.77	245.0±122.7	259.2±231.2	0.45
Segment 3 (cm^3)	158.5±99.6	192.5±161.4	0.01	173.9±113.6	186.8±162.8	0.36	170.3±113.8	189.2±152.8	0.21
Segment 4 (cm^3)	234.1±170.0	270.2±147.0	0.04	250.0±137.5	264.8±165.2	0.34	253.9±128.3	257.8±158.8	0.81
Segment 5 (cm^3)	209.7±117.5	241.6±161.5	0.02	226.6±140.1	234.5±155.0	0.60	236.3±148.8	232.8±154.1	0.84
Segment 6 (cm^3)	150.6±132.6	173.5±170.4	0.15	167.3±207.9	167.1±125.8	0.98	140.6±103.2	179.6±174.4	0.01
Segment 7 (cm^3)	232.5±93.9	246.6±130.3	0.22	233.5±110.8	248.6±125.5	0.22	235.8±113.5	251.9±124.0	0.25
Segment 8 (cm^3)	216.5±103.5	227.7±106.1	0.32	217.1±106.0	229.3±105.3	0.27	227.5±103.2	228.3±107.1	0.95
Liver volume with bodyweight adjustment									
TLV:BW (cm^3:kg)	17.8±7.0	20.7±9.9	0.0009	19.3±6.8	20.3±10.4	0.25	20.5±13.2	19.3±7.2	0.40
FLV:BW (cm^3:kg)	17.5±6.8	20.0±9.6	0.002	18.8±6.5	19.6±10.1	0.32	19.9±12.8	18.7±6.9	0.41
Segment 1:BW (cm^3/kg)	0.5±0.4	0.6±0.6	0.04	0.6±0.5	0.6±0.6	0.38	0.5±0.5	0.6±0.6	0.26
Segment 2:BW (cm^3/kg)	3.0±1.9	3.2±2.6	0.51	3.1±1.5	3.2±2.8	0.66	3.2±2.6	3.0±2.2	0.51
Segment 3:BW (cm^3/kg)	1.9±1.4	2.4±2.2	0.01	2.1±1.4	2.3±2.3	0.22	2.3±2.4	2.2±1.8	0.79
Segment 4:BW (cm^3/kg)	2.7±1.9	3.3±2.1	0.005	3.0±1.8	3.2±2.2	0.26	3.3±2.4	3.0±1.9	0.35
Segment 5:BW (cm^3/kg)	2.4±1.3	2.9±2.0	0.005	2.7±1.6	2.9±2.0	0.36	3.0±2.3	2.7±1.7	0.22
Segment 6:BW (cm^3/kg)	1.8±1.8	2.1±1.8	0.149	1.9±1.9	2.1±1.8	0.47	1.8±1.5	2.1±1.8	0.11
Segment 7:BW (cm^3/kg)	2.8±1.2	3.0±1.9	0.07	2.8±1.3	3.1±1.9	0.07	3.0±2.0	2.9±1.5	0.66
Segment 8:BW (cm^3/kg)	2.5±1.1	2.7±1.4	0.07	2.5±1.2	2.8±1.5	0.10	2.8±1.6	2.6±1.3	0.31
Spleen volume with and without body weight adjustment									
Total spleen volume (cm^3)	800.5±481.5	754.5±522.4	0.39	893.9±521.2	683.7±457.1	<0.0001	813.8±503.7	764.9±515.1	0.42

Variables	Hepatic encephalopathy			Esophageal varices			Ascites		
	Yes (N = 120)	No (N= 274)	p-value	Yes (N=142)	No (N=248)	p-value	Yes (N=89)	No (N=285)	p-value
Functional spleen volume (cm^3)	777.7±469.5	730.8±505.7	0.37	868.2±509.0	661.4±440.2	<0.0001	788.5±487.5	742.4±501.0	0.44
Total spleen volume:BW (cm^3/kg)	9.1±5.3	9.1±7.6	0.91	10.4±5.9	8.2±7.4	0.001	10.5±10.5	8.6±5.6	0.09
Functional spleen volume:BW (cm^3/kg)	8.9±5.1	8.8±7.4	0.88	10.1±5.7	8.0±7.2	0.001	10.2±10.1	8.3±5.4	0.10
Total liver to spleen ratio	3.0±4.3	**3.5**±3.2	0.22	2.4±1.5	3.9±4.2	0.26	2.7±1.9	3.5±3.9	0.01
Functional liver to spleen ratio	3.0±4.3	3.5±3.1	0.29	2.4±1.5	3.9±4.2	<0.0001	2.7±1.9	3.5±3.9	0.008

* only reported cases with available data on the complications of portal hypertension

Table 5:

Baseline characteristics, laboratory values, and liver volume measurements stratified by outcomes during follow up.

Variables	Alive (N=319)	Transplanted (N=111)	p-value
Age (Yrs)	55.7±10.1	53.4±10.0	0.03
Body weight (Kg)	87.2±20.5	88.7±19.8	0.50
Height (cm)	170.2±13.6	172.6±14.0	0.11
Body mass index (kg/m^2)	30.6±13.0	30.1±8.5	0.67
White blood cell counts (×10^3/mm^3)	5.7±3.0	5.2±4.1	0.24
Hemoglobin (g/dl)	12.6±3.0	12.0±2.4	0.04
Platelet counts (×10^3/mm^3)	120.5±84.5	88.6±44.4	<0.0001
Creatinine (mg/dl)	1.1±1.4	1.0±0.9	0.18
Total bilirubin (mg/dl)	2.2±3.0	2.6±1.9	0.14
Alanine aminotransferase (ALT, U/L)	56.2±106.7	53.6±63.4	0.76
Aspartate aminotransferase (AST, U/L)	77.2±134.2	78.5±71.8	0.89
Alkaline phosphatase (ALP, U/L)	125.1±96.1	142.7±92.7	0.09
Albumin (g/dl)	3.1±0.6	3.0±0.7	
Total protein (g/dl)	7.2±4.2	7.0±0.9	0.26
International normalized ratio (INR)	1.3±0.8	2.9±15.3	0.28
MELD scores	10.4±6.0	12.2±7.1	0.01
Total liver volume (TLV, cm^3)	1736.4±610.4	1514.8±534.0	0.0004
Functional liver volume (FLV, cm^3)	1676.4±602.6	1482.9±490.0	0.001
Segment 1 volume (cm^3)	45.9±49.1	42.0±42.4	0.43
Segment 2 volume (cm^3)	257.5±126.0	278.2±336.4	0.52
Segment 3 volume (cm^3)	201.9±157.0	162.7±104.1	0.003
Segment 4 volume (cm^3)	261.0±153.0	235.4±126.3	0.08
Segment 5 volume (cm^3)	248.1±155.6	206.5±118.0	0.004
Segment 6 volume (cm^3)	175.2±146.8	147.8±97.4	0.02
Segment 7 volume (cm^3)	268.4±136.7	226.6±104.6	0.001
Segment 8 volume (cm^3)	245.2±105.1	216.8±100.9	0.01
Total volume:body weight (cm^3:kg)	20.7±9.2	17.7±7.7	0.0009
functional volume:body weight (cm^3:kg)	20.0±9.1	17.3±7.2	0.002
Segment 1:BW (cm^3/kg)	0.5±0.6	0.5±0.5	0.41
Segment 2:BW (cm^3/kg)	3.1±1.9	3.2±3.1	0.74
Segment 3:BW (cm^3/kg)	2.4±2.2	1.9±1.3	0.001
Segment 4:BW (cm^3/kg)	3.1±2.1	2.7±1.7	0.04
Segment 5:BW (cm^3/kg)	2.9±1.9	2.4±1.5	0.004
Segment 6:BW (cm^3/kg)	2.1±1.6	1.7±1.3	0.04

Variables	Alive (N=319)	Transplanted (N=111)	p-value
Segment 7:BW (cm^3/kg)	3.2±1.7	2.7±1.4	0.002
Segment 8:BW (cm^3/kg)	2.9±1.3	2.5±1.3	0.01
Total spleen volume (cm^3)	778.9	946.9±594.6	0.008
Functional spleen volume (cm^3)	754.6	916.2±576.7	0.008
Total spleen volume:BW (cm^3/kg)	9.3±7.6	10.8±6.5	0.05
Functional spleen volume:BW (cm^3/kg)	9.0±7.4	10.4±6.3	0.05
Total liver to spleen ratio	3.3±2.9	2.2±1.5	<0.001
Functional liver to spleen ratio	3.3±2.9	2.2±1.5	<0.001